

9 February 1953

Dr. Joshua Lederberg  
Department of Genetics  
University of Wisconsin  
Madison, Wisconsin.

Dear Dr. Lederberg,

As a medical man and a biochemist who has found himself adrift in unfamiliar waters, I seek your advice in a matter.

As I stated to you when I last sent you a copy of the manuscript on the copper organism, I had already sent it into the Jour of General Physiology at the suggestion of Dr. Smadel. In a sentence it was rejected in a letter from Mirsky. He stated merely that it was premature. Dr. Warren, the head of our department, then picked it up and sent it off to a Dr. Porter at the Department of Bacteriology in Iowa - presumably to the Journal of Bacteriology. The wisdom of this move is not to be discussed here; the results of the move, however, are to be discussed from what I might learn. Enclosed is a copy of the manuscript and the comments.

I bother you in this matter for several reasons. First I wanted you to realize that I did not thoughtlessly ignore your criticisms - I had unfortunately not gotten in touch with you before it was first sent off. Second I would like to know how you would tackle this business of ruling out or in selection. What do you think of this added variable of the streptomycin resistance and what are the details of such a reconstruction experiment. Thirdly, would you hold up all other things before this point of selection was absolutely sure? You see, as an outsider looking in I am impressed with the disagreement among the experts as to what really proves the point.

Fourthly, in this matter of exact correlation between direct and plate counts, I found thru discussions with Monod and Woods that I am not alone. I am the first to admit that you can get nice sigmoid curves with plate counts, but the correlation with the direct is what I find difficult - at least to a point of accuracy that would justify applying my nucleic acid data to them.

Fifthly, though not elegant, do you agree that the ultra violet work is inadequate? Sixth - do you feel the nucleic acid data is unconvincing -

Finally do you think reference to Eprussi should be left out? I do not mention it repeatedly. Furthermore I have discussed this whole thing with Eprussi in great detail and he has given nothing but encouragement. I certainly realize the differences.

Of course the comment about biased planning is ridiculous. I read those references and wrote that paragraph after the work was all done. Having had most of my dealings with the JBC in the past this last comment struck me as peculiarly unconstructive and not very objective. I rather agree with the person, that there are good arguments for leaving such a paragraph out.

In addition to these specific questions, the overall problem is this. I am engaged in very time consuming research with viruses. I have the new nucleotide isolated in the diphosphate form and am doing enzyme studies on it. Also Seymour and I are engaged in experiments involving host transfer in the light of this new compound. We grow the bugs in Phila and I bring everything down here and work on it. The present experiments involving differential labeling of the pyrimidines of the host are most exciting, but very time consuming from the chemistry point of view. Also I have considerable teaching responsibilities in math and medicine every day and my lab and technical help are limited. These of course are not reasons for pushing unfinished work, but they do present a dilemma. Do you think that a few definitive experiments in this <sup>copper</sup> matter are feasible in my next five months here, or do you think that the matter best be dropped completely. I feel rather badly about the fact that I may have conveyed to various members of your specialty an attitude of irresponsibility and lack of understanding for the difficulties involved. On the other hand I do not want to ignore what might be a significant finding in your field, anymore than I would think of ignoring a new pyrimidine, for example.

I am now measuring increasing 260 absorption during that first period in the presence of copper - a period when cell counts fall (on plates) and when visible density remains unchanged. Other than this I am not working with the coli - and will not until I hear from you. It is bad enough to spread yourself thin even when you think you know what you are doing - to say nothing of the times when you do not.

I am sorry I cannot take you up on an extended visit. I am leaving the army in July to take a residency at Hopkins. My real aim is to someday bring basic science on to the wards with the medical students and internes, so the year away from research is necessary.

I sure would appreciate your opinions as to how to expand this <sup>copper</sup> information or better what to do with it or where to dump it.

Looking forward to the day when the bridge, from the island of nucleic acid chemistry into the glorious ~~ly~~ field of genetics, will be a little broader and a little more secure.

Thanks for your reprints. I shall send you some the next time I visit Penn <sup>and</sup> replenish my supply. A toothbrush and a car to get home are the main things I keep here with me in the army.

Sincerely,

LARRY *Ches*